regimens that minimize infusion frequency. Cefazolin, cefonicid sodium, cefoperazone sodium and ceftriaxone sodium are used extensively because their infrequent dosing requirements, safety and spectrum match many conditions amenable to home therapy.

A competent, effective IV therapy team is another critical component of this technique. IV therapists need to have both expert nursing skills and knowledge regarding potential toxicity. They must remain readily available to patients on a 24-hour basis and possess strong teaching skills so that patients develop confidence and judgment.

Issues still to be standardized are the optimal organization of home care agencies, patient and diagnosis qualification criteria, standards of care for physicians and agencies, reimbursement and liability exposure.

In the final analysis, home IV therapy makes sense in today's thrust toward providing as much care as is safe and feasible outside hospital. It synergizes with the public impulse to accept more responsibility for personal fitness and health. To invoke this new modality, physicians need only blend their current expertise and sound medical judgment with the special considerations for home therapy summarized above. When home IV antibiotic therapy is done well, everyone benefits.

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Vaccination for Hepatitis B

TWO SAFE VACCINES containing purified hepatitis B surface antigen (HBsAg) are now available for preventing hepatitis B infection. The first vaccine is derived from the plasma of screened, healthy HBsAg carriers. Even though extensive tests show that all known viruses are inactivated by the vaccine preparation process, many patients and health care providers have been reluctant to use this plasma-derived vaccine because of concerns about the acquired immunodeficiency syndrome. The second vaccine, released in early 1987, is prepared from recombinant DNA propagated in yeast. The recombinant vaccine, because it is not plasma derived, has had greater acceptance but has no other advantages and has a similar level of safety and cost. Concerns about long-term efficacy of the yeast-recombinant vaccine have been raised because of reduced antigenicity when compared with plasma-derived HBsAg.

Protective levels of antibody to HBsAg develop in about 85% to 95% of vaccinated healthy adults, who receive three doses of vaccine intramuscularly in the deltoid. Antibody levels tend to be lower if the injections are given in the buttock or to patients who are immunologically compromised. For those who have the usual anti-HBsAg response, protection approaches 100%. The duration of protective antibody levels is not yet known and booster doses may be required at some future time.

There are no known adverse or beneficial effects to vaccinating previously infected persons. Thus, the decision to screen potential vaccinees (using either hepatitis B core antigen or anti-HBsAg) is an economic one, based on the cost of screening tests and vaccination versus the likelihood that a patient has previously had hepatitis B.

Hepatitis B vaccine is recommended for persons at increased risk of hepatitis B developing. Potential vaccinees include homosexually active men, users of illicit injectable drugs, hemodialysis patients, selected immigrants, prisoners, institutionalized retarded persons, recipients of factor VIII or IX concentrates, long-term transfusion recipients, household and sexual contacts of hepatitis B carriers and health care workers with frequent exposure to blood or blood products.

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Intraperitoneal Chemotherapy for Ovarian Cancer

OVARIAN CANCER is the most common fatal gynecologic malignant disorder in the United States and the fourth leading cause of cancer death in women, with 18,000 new cases and 11,000 deaths per year. About 80% of patients with ovarian cancer have advanced disease (stage III or IV) at diagnosis. With the introduction of cisplatin-based combination chemotherapy administered systemically, surgically documented complete response rates of 20% to 30% can now be achieved. Few of these responses, however, result in long-term relapse-free survival (seven-year survival rate less than 15%).

Ovarian cancer is a disease that tends to remain confined to the peritoneal cavity even in its most advanced stages. This makes it particularly amenable to regional methods of drug delivery. A recently developed technique for treating advanced ovarian cancer has been the direct intraperitoneal administration of chemotherapeutic agents. One of the major principles of intraperitoneal chemotherapy is to administer the anticancer agent in a large fluid volume of a normal saline solution (two liters) to ensure adequate drug distribution throughout the peritoneal cavity. Another is to administer agents known to be active against ovarian cancer when administered systemically. With intraperitoneal administration, high drug concentrations can be achieved in the area of the tumor while corresponding systemic levels are much less, resulting in less drug exposure to normal tissues. This results in an enhancement of the drug's therapeutic index. We have used a totally implantable drug delivery system for intraperitoneal drug administration in our studies. It consists of a Tenckhoff catheter attached to a Port-a-Cath portal (Pharmacia Nu Tech).

The most active single agent for the treatment of ovarian cancer is cisplatin. We have conducted a series of intraperitoneal cisplatin-based chemotherapy trials over the past several years. Agents that we have used in combination with cisplatin have included cytarabine and, most recently, etoposide. These studies have been done in patients with persistent disease following administration of at least six cycles of intravenous cisplatin-based chemotherapy. Two important conclusions have emerged from these studies. First, the intra-

peritoneal administration of chemotherapy does not appear to be superior to administering it intravenously in patients with bulky intraperitoneal disease. In patients with small-volume disease (tumor nodules less than 2 cm in diameter), however, the results have been excellent, with 70% of patients alive, with a median follow-up of 29 months and with an apparent plateau on the survival curve. These results are superior to any other published data in patients with refractory ovarian cancer.

These encouraging results need to be confirmed in prospective, randomized clinical trials involving a much larger number of patients. The Southwest Oncology Group is currently conducting a prospective clinical trial in which patients with previously untreated stage III ovarian cancer (disease confined to the peritoneal cavity; tumor nodules less than 2 cm in diameter) are being randomly assigned to intraperitoneal cisplatin-containing chemotherapy or intravenous cisplatin-containing chemotherapy. Many single-arm clinical trials of intraperitoneal chemotherapy have been initiated over the past two years at a number of university medical centers. In addition, based on the above encouraging results, intraperitoneal administration of cisplatin is being more widely used in community practice for ovarian cancer patients with refractory, small-volume disease confined to the peritoneal cavity.

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Bone Marrow Transplantation as Primary Treatment of Leukemia

CONSIDERABLE PROGRESS HAS BEEN MADE during the past ten years in the treatment of acute and chronic myelogenous and acute lymphoblastic leukemia using bone marrow transplantation.

In the initial trial of *allogeneic* bone marrow transplantation in patients with relapsed acute myelogenous leukemia by the Seattle transplant team, a long-term relapse-free survival of 13% was achieved in patients for whom all prior therapies had failed. When patients, however, were transplanted earlier in the course of their disease—in first remission—relapse rates dropped to 15% to 20% and overall survival is now 40% to 50%. Because chemotherapy for acute myelogenous leukemia has been improving and the complications of bone marrow transplantation have remained significant, the role and timing of allogeneic transplantation have been questioned.

The success of allogeneic bone marrow transplantation in the treatment of acute myelogenous leukemia was recently confirmed by three randomized studies of transplantation versus chemotherapy. These studies all show a greatly decreased risk of relapse but considerable mortality due to graft-versus-host disease and concurrent infections following bone marrow transplantation in comparison with consolidation chemotherapy. As a result, overall survival is better following bone marrow transplantation, but the complication rate remains high. Further success will depend on the improved abrogation of graft-versus-host disease and fewer infectious complications. Attempts to decrease graft-versus-host disease by T-cell depletion of the donor marrow have been successful in abrogating the reaction but have unfortunately been complicated by higher rates of fungal infection, a greater risk of graft rejection and a higher risk of leukemic relapse.

Autologous transplantation for patients with acute myelogenous leukemia in both first and second (or third) remission avoids the risk of graft-versus-host disease but has a potentially higher relapse rate than allogeneic bone marrow transplantation. Preliminary results indicate that 25% to 40% of patients in first remission may achieve at least one year of disease-free survival following ablative chemotherapy and reinfusion of marrow harvested and frozen while in remission. Autologous transplantation of marrow purged of residual leukemic cells with 4-hydroperoxycyclophosphamide has resulted in a two-year disease-free survival of 40% for patients with acute myelogenous leukemia in second or third remission.

For patients with chronic myelogenous leukemia there had been no hope for cure and no improvement in survival with any form of standard therapy since George Richards Minot introduced splenic irradiation in the 1920s. Now data clearly show that allogeneic bone marrow transplantation will provide a 50% to 60% relapse-free survival in patients with chronic myelogenous leukemia in chronic phase. Results are better the earlier the transplant is done after diagnosis and when patients are younger than age 30. Especially encouraging is the absence of Philadelphia chromosome-positive cells as long as five years after transplantation. When patients reach the accelerated phase of chronic myelogenous leukemia or an overt blast crisis develops, disease-free survival drops to 15%. Results of autologous transplants for chronic myelogenous leukemia have been uniformly poor thus far. Using partially matched siblings with T-cell depletion of the donor marrow or matched unrelated donors has had limited success, but complications such as increased rates of graft rejection and relapse have limited this to an experimental approach at present.

Allogeneic transplantation for acute lymphoblastic leukemia has not been as successful, primarily because of a high posttransplant relapse rate (60%). Changes in the conditioning chemotherapy regimen may improve the outcome. A relapse-free survival rate of 30% in children in second remission and without human leukocyte antigen-matched donors has been achieved by using monoclonal antibodies to common acute lymphocytic leukemia antigen to deplete autologous marrow of leukemic cells.

The use of improved conditioning regimens to decrease the possibility of relapse, new ways of treating the marrow to purge it of T cells or leukemic cells and enhanced prevention of posttransplant infections will enable more patients with leukemia to be treated successfully. In time, partially matched and unrelated transplants will also become practical. Ultimately, it should become possible to culture pure marrow stem cells, avoiding graft-versus-host disease entirely.

Current recommendations would include allogeneic bone